R.W. JOHNSON PHARM. RES. INST. USA

MEDWATCH FDA

Individual Safety Report
3403980-6-00-01

For use by user-facilities, manufacturers for reporting

— of 3

Approved by FDA on 09/25/95

Mfr report # PRIUSA1999006530

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
?-? In confidence	30 yr ??/???/??	☒ female ☐ male	UNK lbs or UNK kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☒ death ??/???/?? (mo/day/yr)
- ☐ life-threatening
- ☒ hospitalization - initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other:

3. Date of event (mo/day/yr): ??/???/??

4. Date of this report (mo/day/yr): 11/12/99

5. Describe event or problem

Report published in 1991 Annual Report of the American Association of Poison Control Centers National Data Collection System (case 252). A 30-year-old patient (sex unspecified) died following the ingestion of acetaminophen with codeine and chlordiazepoxide, and use of heroin. Serum acetaminophen level 8 mcg/mL. Intent of ingestion is unknown. Exposure to medication was chronic.

Additional information received 11-Nov-99: This 30 year old female with history of heroin and alcohol abuse, a recent hospitalization for terminal liver disease with jaundice, and ascites presented to emergency room awake and alert, but was "unarousable at home", after a possible overdose with 30 tablets of acetaminophen with codeine (#3) and 5 tablets of chlordiazepoxide at an unknown time of ingestion. The patient denied use of diamorphine and ethanol in the last four days. Pupils were "small" on arrival. She again became lethargic at the time of the call to the Poison Control Center from the intensive care unit. Pulse oximetry was 89%.

(Cont.)

6. Relevant tests/laboratory data, including dates

Urine toxicology screen: positive for opiates and benzodiazepines (day 1 of hospitalization), anion gap: 8 (day 6 of hospitalization)
(Lab data cont.)

DSS

NOV 21 1999

ADVERSE EVENT REPORTING SYSTEM

(Cont.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Drug abuse
Heroin and alcohol abuse, a recent hospitalization for terminal liver disease with jaundice, and ascites, positive hepatitis A, and sepsis due to subacute spontaneous peritonitis

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 TYLENOL W/CODEINE NO. 3(tablet)(ACETAMINOPHEN/CODEINE)
#2 LIBRIUM(CHLORDIAZEPOXIDE HYDROCHLORIDE)

2. Dose, frequency & route used
#1 oral
#2 oral

3. Therapy dates (if unknown, give duration) (from/to (or best estimate))
#1 ??/???/??
#2 ??/???/??

4. Diagnosis for use (indication)
#1 UNKNOWN
#2 UNKNOWN

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
1) ZANTAC(RANITIDINE HYDROCHLORIDE)
2) GENTAMICIN(GENTAMICIN)

(Cont.)

D. All manufacturers

1. Contact office - name/address (& mfring site for devices)
R.W. JOHNSON PHARM. RES. INST. USA
DIV. OF ORTHO PHARMACEUTICAL CORP.
920 U.S. Route 202
P.O. Box 300
Raritan NJ 08869
USA
(Informing Unit)

2. Phone number: 908-704-4504

3. Report source (check all that apply)
- ☐ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other:

4. Date received by manufacturer (mo/day/yr): 11/11/99

5. (A)NDA # 85-055
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
- ☐ 5-day ☒ 15-day
- ☐ 10-day ☐ periodic
- ☐ Initial ☒ follow-up # 1

8. Adverse event term(s)
1) HEPATIC FAILURE
2) RENAL FAILURE ACUTE
3) SEPSIS
4) PULMONARY OEDEMA
5) COMA
6) FEVER
7) CONFUSION

(Cont.)

9. Mfr. report number
PRIUSA1999006530

E. Initial reporter

1. Name, address & phone #
Dr. Toby Litovitz
National Capital Poison Center
Georgetown University Hospital
3800 Reservoir Road NW
Washington, DC 20007
USA

NOV 19 1999

2. Health professional? ☒ yes ☐ no

3. Occupation: Physician

4. Initial reporter also sent report to FDA ☐ yes ☐ no ☒ unk

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

3500A Facsimile

R.W. PHARM. RES. INST. USA
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uation Sheet for FDA-3500A Form — of 3

Mfr report # : PRIUSA1999006536

Date of this report : 11/12/99

B. Adverse event or product problem

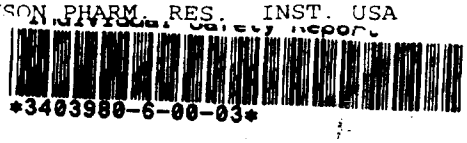
B.5 Describe event or problem (Cont...)

She also had a high fever. She had been lavaged, and given charcoal and cathartic and was on 02. Admission plasma acetaminophen level was 8 mcg/mL. The Poison Control Center provided advisement to check for lab error, repeat the level; and that N-acetylcysteine was not necessary with this acetaminophen level. A repeat plasma acetaminophen level three hours after the first level was 6.2mcg/mL. Urine was positive for opiates and benzodiazepines only. She had a positive response to naloxone. The physician felt the patient may have subacute pericarditis/sepsis. Patient developed pulmonary edema, continued to be febrile, became more confused, and eventually became comatose and jaundiced. She was labeled a no code status due to previous history of terminal liver disease. She developed hepato-renal failure and expired on day 14 of hospitalization. The physician felt the patient initially overdosed on chlordiazepoxide, but due to the liver failure, it was metabolized slowly. Additional history from the family indicated she didn't overdose on acetaminophen with codeine, but took a couple of tablets q2h 'every so often'. Patient also had positive hepatitis A and sepsis due to subacute spontaneous peritonitis. The Poison Control Center's toxicologist felt the acetaminophen could be a toxicologically contributing factor to her disease.

B.6 Relevant tests/laboratory data, including dates (Cont...)

Lab Result :

Sl.No.	Test date	Test name	Test result	Normal value
1	??/???/??	ALANINE AMINOTRANSFERASE	12 IU/L (international unit/liter)	
		(day 2 of hospitalization) ALBUMIN	1.9 g/L (grams/liter)	
		(day 2 of hospitalization) ALKALINE PHOSPHATASE	351 IU/L (international unit/liter)	
		(day 2 of hospitalization) ALKALINE PHOSPHATASE	259 IU/L (international unit/liter)	
		(day 6 of hospitalization) AMMONIA	38 g/dL (grams/deciliter)	
		(day 2 of hospitalization) ASPARTATE AMINOTRANSFERASE	265 IU/L (international unit/liter)	
		(day 2 of hospitalization) ASPARTATE AMINOTRANSFERASE	1600 IU/L (international unit/liter)	
		(day 6 of hospitalization) BILIRUBIN, TOTAL	5.2 mg/dL (milligram/deciliter)	
		(day 1 of hospitalization) BILIRUBIN, TOTAL	8.3 mg/dL (milligram/deciliter)	
		(day 6 of hospitalization) BLOOD UREA NITROGEN	9 mg/dL (milligram/deciliter)	
		(day 4 of hospitalization) BLOOD UREA NITROGEN	12 mg/dL (milligram/deciliter)	
		(day 6 of hospitalization) BLOOD UREA NITROGEN	15 mg/dL (milligram/deciliter)	
		(day 9 of hospitalization) CARBON DIOXIDE	34 mmHg (millimeter mercury)	
		(day 9 of hospitalization) CHLORIDE	100 mEq/L (milliequivalent/-liter)	
		(day 9 of hospitalization) CREATININE	0.6 mg/dL (milligram/deciliter)	
		(day 4 of hospitalization) CREATININE	0.7 mg/dL (milligram/decili-	



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	ter)
(day 6 of hospitalization) CREATININE	0.6 mg/dL (milligram/decili-ter)
(day 9 of hospitalization) DRUG LEVEL	8 mcg/mL (microgram/millil-iter)
acetaminophen level (on admission) DRUG LEVEL	6.2 mcg/L (microgram/liter)
acetaminophen level three hours after the first level DRUG LEVEL	2.2 mcg/L (microgram/liter)
(day 2 of hospitalization) GAMMA GLUTAMYL TRANSFERASE	310 IU/L (international unit/liter)
(day 2 of hospitalization) GAMMA GLUTAMYL TRANSFERASE	164 IU/L (international unit/liter)
(day 6 of hospitalization) HAEMOGLOBIN	9.6 g/dL (grams/deciliter)
(day 9 of hospitalization) POTASSIUM	4.6 mEq/L (milliequivalent/-liter)
(day 5 of hospitalization) POTASSIUM	3.7 mEq/L (milliequivalent/-liter)
(day 9 of hospitalization) RED BLOOD CELL/COUNT	2.72 L (liter)
(day 9 of hospitalization) SODIUM	137 mEq/L (milliequivalent/-liter)
(day 9 of hospitalization) WHITE BLOOD CELL/COUNT	19,500 L (liter)
(day 9 of hospitalization)	

C10. Concomitant medical products

Seq No. : 1
Concomitant Medical Product : ZANTAC(RANITIDINE HYDROCHLORIDE)
Dose, frequency & route used : 1) oral

Seq No. : 2
Concomitant Medical Product : GENTAMICIN(GENTAMICIN)
Dose, frequency & route used : 1) oral

G. All manufacturers

8. Adverse event term(s)

8) DRUG ABUSE

Source of report (Literature):

Seq No. : 1
Author : Toby Litovitz
Journal title : 1991 Annual Report of the American Association of Poison Control Centers National Data Collection System
Year : 92
Edition : 10(5)
Page number : From 452 To 505
Article title : American Journal of Emergency Medicine